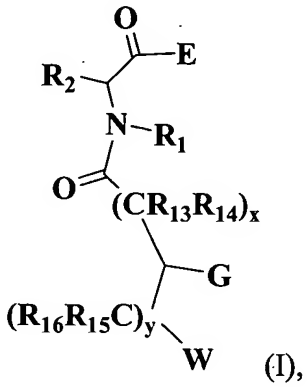
Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of claims:

1. (Currently amended) A compound of formula (I),

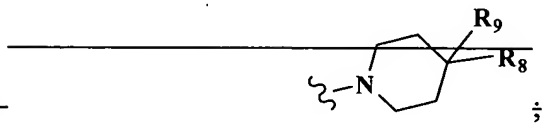


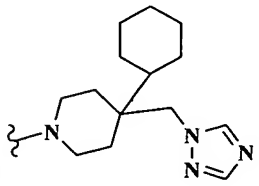
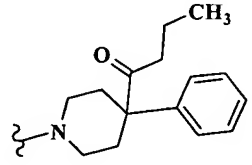
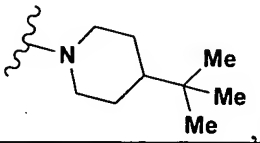
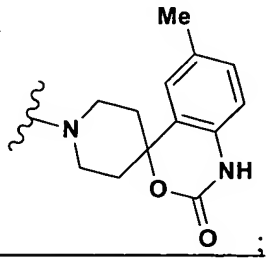
(I),

or a pharmaceutically-acceptable salt or hydrate, thereof, in which:

R_1 is hydrogen or $C_{1\text{-}6}$alkyl or is taken together with R_2 or R_3 to form a monocyclic or bicyclic aryl, cycloalkyl, heteroaryl or heterocycle;

R_2 is $C_{1\text{-}6}$alkyl or $C_{2\text{-}6}$alkenyl optionally substituted with one to three-aryl, cycloalkyl, or heteroaryl, provided that where G is $C_{2\text{-}6}$alkenyl, A_1–$NR_{18}CO_2R_{19}$, or A_1–SO_2R_{17}, or when y is 0, R_2 may be or $C_{1\text{-}6}$alkyl or $C_{2\text{-}6}$alkenyl, each optionally substituted with heteroaryl;

~~E is~~  ~~;~~

E is  ,  ,  , or  ;

G is selected from A_1–$NR_{18}C(=O)R_{19}$; A_1–$NR_{18}SO_2R_{17}$, A_1-$NR_{18}CO_2R_{19}$, and A_1–$NR_{20}C(=O)NR_{18}R_{19}$ wherein A_1 is a bond, $C_{1\text{-}6}$alkylene, or $C_{2\text{-}6}$alkenylene, or where G is A_1–$NR_{18}CO_2R_{19}$, or when y is 0, R_2 may be $C_{1\text{-}6}$alkyl or $C_{2\text{-}6}$alkenyl, each substituted with heteroaryl;

W is selected from substituted or unsubstituted heterocyclo, heteroaryl, or cycloalkyl selected from azetidinyl and imidazolyl~~, wherein said heteroaryl, heterocyclo or cycloalkyl groups may additionally have joined thereto an optionally substituted five-to-seven membered heterocyclic, heteroaryl, or carbocyclic ring~~;

~~R_8 and R_9 are selected independently from hydrogen, alkyl, $-(CH_2)_j-C(=O)$alkyl, $-(CH_2)_j-$phenyl, $-(CH_2)_j-$napthyl, $-(CH_2)_j-C_{4-7}$cycloalkyl, $-(CH_2)_j-$heterocyclo, and $-(CH_2)_j-$heteroaryl, provided R_8 and R_9 are not both hydrogen, or R_8 and R_9 together form a spirocycloalkyl or spiroheterocyclic ring; and~~

~~*j* is selected from 0, 1, 2 and 3.~~

~~R_{10} is selected from hydrogen, alkyl, substituted alkyl, cycloalkyl, aryl, heteroaryl, and hetereocyclo;~~

~~R_{11} is hydrogen or C_{1-8}alkyl;~~

~~R_{12} is C_{1-8}alkyl, substituted C_{1-8}alkyl, or cycloalkyl;~~

R_{13}, R_{14}, R_{15} and R_{16} are selected independently of each other from hydrogen, alkyl, substituted alkyl, amino, alkylamino, hydroxy, alkoxy, aryl, cycloalkyl, heteroaryl, or heterocyclo, or R_{13} and R_{14}, or R_{15} and R_{16}, when attached to the same carbon atom, may join to form a spirocycloalkyl ring;

R_{17} is alkyl, substituted alkyl, cycloalkyl, aryl, heterocyclo, or heteroaryl;

R_{18}, R_{19}, and R_{20} are independently selected from hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, aryl, heteroaryl, cycloalkyl, heterocyclo, or $C(=O)R_{28}$; or when G is $NH(C=O)R_{19}$, R_{19} may be a bond joined to W to define a heterocyclo ring; provided, however, that when *y* is at least one, W is imidazolyl~~, indolyl, $-NR_{21}R_{22}$, or $-OR_{23}$~~, and G is $-NR_{18}C(=O)R_{19}$, then R_{19} is not a C_1-alkyl having the substituent $-NR_{29}R_{31}$;

~~R_{21} and R_{22} are selected from hydrogen, alkyl, and substituted alkyl;~~

~~R_{23} and R_{24} are independently hydrogen, alkyl, substituted alkyl, aryl, heteroaryl, heterocyclo, and cycloalkyl;~~

~~R_{25}, R_{26} and R_{27} are independently hydrogen, alkyl, substituted alkyl, cycloalkyl, aryl, heterocyclo, or heteroaryl; or R_{25} and R_{26} may join together to form a heterocyclo or heteroaryl, except R_{26} is not hydrogen when joined to a sulfonyl group as in $-S(O)_pR_{26}$ or $-NR_{25}SO_2R_{26}$;~~

~~R_{28} is hydrogen, alkyl, or substituted alkyl;~~

R_{29} and R_{31} are selected from hydrogen, alkyl, haloalkyl, hydroxyalkyl, phenylalkyl, and alkoxycarbonylalkyl, or R_{29} and R_{31} taken together form a heterocyclo ring;

~~*n* is 0, 1, 2, 3 or 4;~~

~~*p* is 1, 2, or 3;~~

x is 0, 1, or 2; and

y is 0, 1, 2, 3 or ~~4; and~~

~~*z* is 0, 1, or 2~~.

2. (Previously presented) A compound according to claim 1, or a pharmaceutically-acceptable salt or hydrate, thereof, in which:

G is selected from:

a) $-NR_{18}C(=O)R_{19}$;

b) C_{1-6}alkylene or C_{2-6}alkenylene joined to one of $-NR_{18}C(=O)R_{19}$, $-NR_{18}CO_2R_{19}$, $-NR_{18}SO_2R_{17}$, and $-NR_{20}C(=O)NR_{18}R_{19}$;

R_{17} is C_{1-4}alkyl, C_{5-6}cycloalkyl, phenyl, or benzyl;

R_{18}, R_{19}, and R_{20} are independently selected from hydrogen, $-C_{1-4}$alkyl, phenyl, benzyl, C_{5-6}cycloalkyl, $-C(=O)CH_2$(phenyloxy), $-C(=O)CH_2$(benzyloxy), imidazolyl, pyridyl, furyl, thienyl, or C_{1-4}alkyl or C_{2-4}alkenyl substituted with one of phenyl, pyridyl, furyl, cyclopentyl, cyclohexyl, CO_2Me, phenyloxy, or benzyloxy, wherein each ringed group of R_{18}, R_{19}, and R_{20} in turn is optionally substituted with one to two R_{36}, and/or optionally has a benzene ring or five membered heterocyclo having two oxygen atoms fused thereto; and

R_{36} is halogen, methoxy, nitro, phenyl, phenyloxy, or alkylamino.

3. (Previously presented) A compound according to claim 2, or a pharmaceutically-acceptable salt or hydrate, thereof, in which

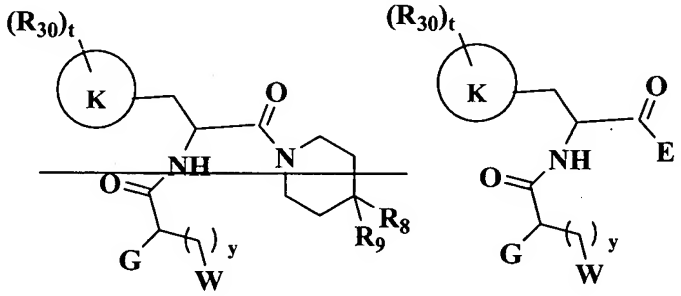
G is $-NR_{18}C(=O)R_{19}$,

R_{18} is hydrogen or lower alkyl, and

R_{19} is C_{1-4}alkyl, C_{2-4}alkenyl, phenyl, benzyl, C_{5-6}cycloalkyl, -C(=O)CH_2(phenyloxy), -C(=O)CH_2(benzyloxy), imidazolyl, pyridyl, furyl, thienyl, or C_{1-4}alkyl or C_{2-4}alkenyl substituted with one of phenyl, phenyl, pyridyl, furyl, cyclopentyl, cyclohexyl, CO_2Me, phenyloxy, and benzyloxy, wherein each ringed group of R_{19} in turn is optionally substituted with one to two R_{36}, and/or optionally has a benzene ring or five membered heterocyclo having two oxygen atoms fused thereto.

4. (Currently amended) A compound according to claim 2, or a pharmaceutically-acceptable salt or hydrate, thereof, in which W is azetidinyl[,] or imidazolyl.

5. (Currently amended) A compound according to claim 1, or a pharmaceutically-acceptable salt or hydrate, thereof, having the formula:



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in which

K is phenyl or thiazolyl;

R_{30} is selected from C_{1-4}alkyl, hydroxy, alkoxy, halogen, nitro, cyano, amino, alkylamino, phenyl, and –C(=O)phenyl;

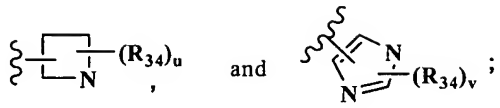
t is 0, 1 or 2; and

y is 0, 1 or 2.

6. (Canceled)

7. (Currently amended) A compound according to claim 1, or a pharmaceutically-acceptable salt or hydrate, thereof, in which

W is a ring selected from:

 and ;

R_{34} at each occurrence is attached to any available carbon or nitrogen atom of W and is selected from C_{1-6}alkyl~~, halogen, amino, aminoalkyl, alkylamino, hydroxy, C_{1-4}alkoxy, hydroxyC_{1-4}alkyl, –C(=O)alkyl, –C(=O)aminoalkyl, –C(=O)phenyl, –C(=O)benzyl, –CO_2alkyl, –CO_2phenyl, –CO_2benzyl, –SO_2alkyl, –SO_2aminoalkyl, –SO_2phenyl, –SO_2benzyl, phenyl, benzyl, phenyloxy, benzyloxy, pyrrolyl, pyrazolyl, piperidinyl, pyridinyl, pyrimidinyl, and tetrazolyl, and/or two R_{34} when attached to two adjacent carbon atoms or adjacent carbon and nitrogen atoms may be taken together to form a fused benzo, heterocyclo, or heteroaryl ring, and/or two R_{34} when attached to the same carbon atom (in the case of a non-aromatic ring) may form keto (=O), and each R_{34} in turn is optionally substituted with up to two R_{35};~~

~~R_{35} is selected from halogen, trifluoromethyl, C_{1-4}alkyl, cyano, nitro, trifluoromethoxy, amino, alkylamino, aminoalkyl, hydroxy, and C_{1-4}alkoxy;~~

~~*w* is selected from 0, 1, or 2;~~

u is selected from 0, 1, 2, and 3; and

v is 0, 1 or 2.

8. – 9. (Canceled)

10. (Previously presented) A compound according to claim 1, or a pharmaceutically-acceptable salt or hydrate, thereof, in which

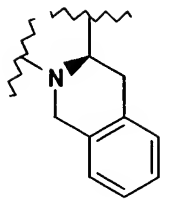
R_2 is selected from C_{1-6}alkyl, C_{2-6}alkenyl~~, C_{2-6}alkenylene-K~~, and –$(CH_2)_g$-K;

K is selected from phenyl, napthyl, thienyl, thiazolyl, pyridinyl, pyrimidinyl, and C_{5-6}cycloalkyl, wherein each group K in turn is optionally substituted with one to three R_{30} or has a benzene ring fused thereto, which also may be substituted with one to three R_{30};

R_{30} is selected from C_{1-4}alkyl, hydroxy, alkoxy, halogen, nitro, cyano, amino, alkylamino, phenyl, and acylphenyl; and

g is 0, 1, 2 or 3.

11. (Currently amended) A compound according to claim 1, or a pharmaceutically-acceptable salt or hydrate, thereof, in which –N(R_1)-CH(R_2)- taken together are selected from ~~C_{1-4}alkylene~~,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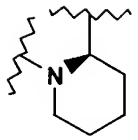
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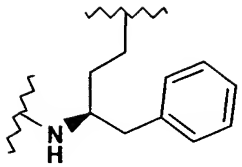
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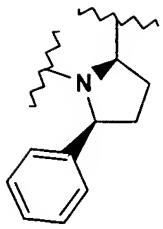
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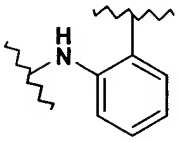
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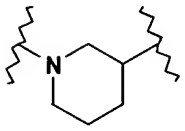
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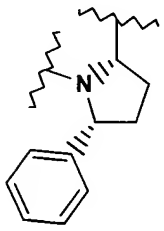
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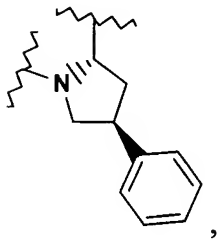
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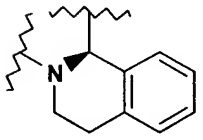
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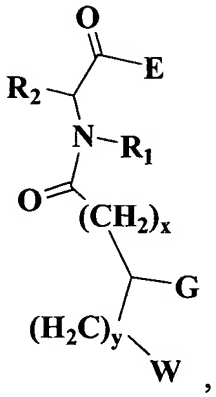
12. (Previously presented) A compound according to claim 1, or a pharmaceutically-acceptable salt or hydrate, thereof, in which

R_1 is hydrogen or C_{1-4}alkyl.

13. (Canceled)

14. (Currently amended) A compound having the formula,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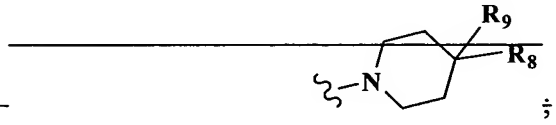
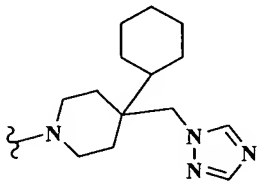
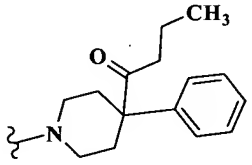
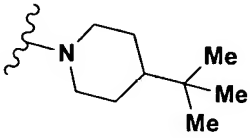
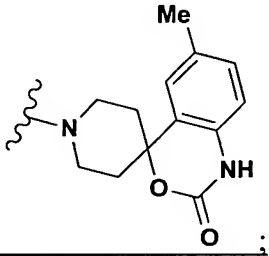
or a pharmaceutically-acceptable salt or hydrate, thereof, in which:

R_1 is hydrogen or C_{1-6}alkyl or is taken together with R_2 or R_3 to form a monocyclic or bicyclic aryl, cycloalkyl, heteroaryl or heterocycle;

R_2 is C_{1-6}alkyl or C_{2-6}alkenyl optionally substituted with one to three-aryl, cycloalkyl, or heteroaryl, provided that where G is C_{2-6}alkenyl, or $[A_1]$–$NR_{18}CO_2R_{19}$, ~~or A_1–SO_2R_{17}~~ or when y is 0, R_2 may be or C_{1-6}alkyl or C_{2-6}alkenyl, each optionally substituted with heteroaryl;

~~E is~~  ;

E is  ,  ,  , or  ;

G is selected from:

a) $NR_{18}C(=O)R_{19}$;

b) C_{1-6}alkylene or C_{2-6}alkenylene joined to one of $-NR_{18}C(=O)R_{19}$, $-NR_{18}CO_2R_{19}$, $-NR_{18}SO_2R_{17}$, and $-NR_{20}C(=O)NR_{18}R_{19}$;

W is selected from –substituted or unsubstituted heterocyclo, heteroaryl, or cycloalkyl selected from azetidinyl and imidazolyl~~, wherein said heteroaryl, heterocyclo or cycloalkyl groups may additionally have joined thereto an optionally substituted five-to-seven membered heterocyclic, heteroaryl, or carbocyclic ring~~;

~~R_8 and R_9 are selected independently from hydrogen, alkyl, $-(CH_2)_j$-C(=O)alkyl, $-(CH_2)_j$-phenyl, $-(CH_2)_j$-napthyl, $-(CH_2)_j$-C_{4-7}cycloalkyl, $-(CH_2)_j$-heterocyclo, and $-(CH_2)_j$-heteroaryl, provided R_8 and R_9 are not both hydrogen, or R_8 and R_9 together form a spirocycloalkyl or spiroheterocyclic ring; and~~

~~*j* is selected from 0, 1, 2 and 3.~~

~~R_{10} is selected from hydrogen, alkyl, substituted alkyl, cycloalkyl, aryl, heteroaryl, and hetereocyclo;~~

~~R_{11} is hydrogen or C_{1-8}alkyl;~~

~~R_{12} is C_{1-8}alkyl, substituted C_{1-8}alkyl, or cycloalkyl;~~

R_{17} is alkyl, substituted alkyl, cycloalkyl, aryl, heterocyclo, or heteroaryl;

R_{18}, R_{19}, and R_{20} are independently selected from hydrogen, alkyl, alkenyl, aryl, heteroaryl, cycloalkyl, heterocyclo, $C(=O)R_{28}$ or a C_{1-4}alkyl or C_{2-4}alkenyl substituted with one or more of aryl, heteroaryl, cycloalkyl, heterocyclo, alkoxycarbonyl, phenyloxy, and/or benzyloxy, and each of said ringed groups of R_{18}, R_{19}, and R_{20} in turn is optionally substituted with one to two R_{36};

R_{21} and R_{22} are selected from alkyl and substituted alkyl;

~~R_{23} and R_{24} are independently selected from hydrogen, alkyl, substituted alkyl, aryl, heteroaryl, heterocyclo, and cycloalkyl;~~

~~R_{28} is hydrogen, alkyl, or substituted alkyl;~~

R_{36} is halogen, methoxy, nitro, phenyl, phenyloxy, or alkylamino;

~~*n* is 0, 1, 2, 3 or 4;~~

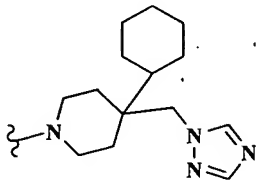
x is 0, 1, or 2; and

y is 0, 1, 2, 3 or 4~~; and~~

~~*z* is 0, 1, or 2~~.

15. (Canceled)

16. (Previously presented) A compound according to claim 14, or a pharmaceutically-acceptable salt or hydrate, thereof, in which E is



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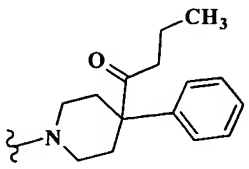
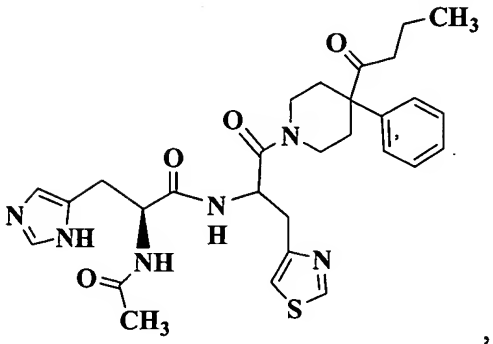


17. (Previously presented) A compound according to claim 14, or a pharmaceutically-acceptable salt or hydrate, thereof, in which G is NHC(=O)(alkyl) or NHC(=O)phenyl.

18. (Previously presented) A compound according to claim 1, having the formula,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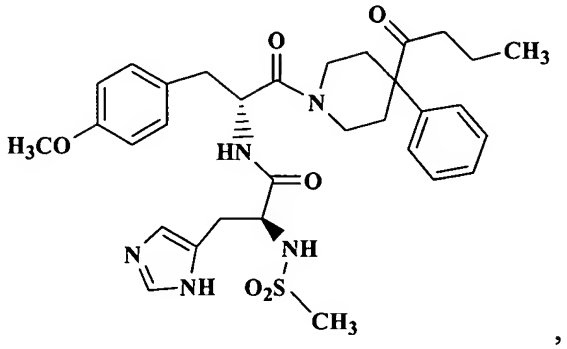
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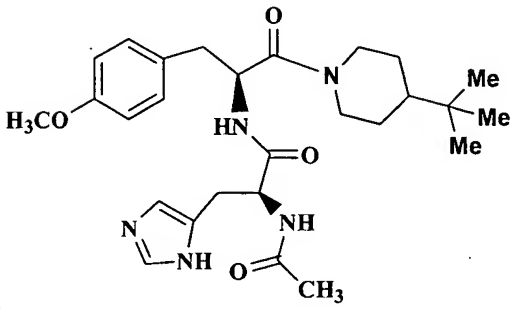
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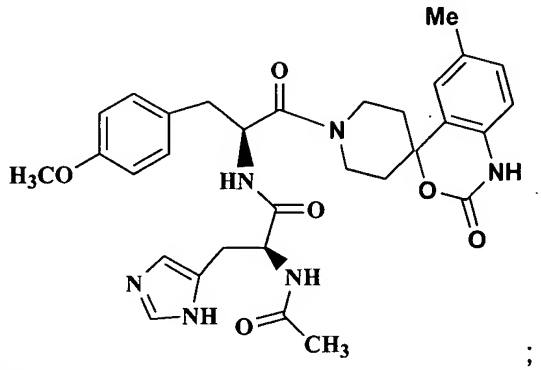
, or ; or a pharmaceutically-acceptable salt or hydrate, thereof.

19. (Previously presented) A pharmaceutical composition comprising at least one compound according to claim 1 or a pharmaceutically-acceptable salt or hydrate, thereof; and a pharmaceutically-acceptable carrier or diluent.

20. – 23. (Canceled)